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The 21st Century Cures Act: Allowing The FDA To Address Modern Value Communication Needs

How to prove the real – and implicit – economic value of pharma products to payers and other stakeholders while FDA regulatory approvals adhere to a historically rigid standard of proof based on randomized tests against placebo in a controlled patient population? The 21st Century Cures Act may finally be extending a new path forward that offers legislative endorsement for use of a greater variety of evidence. What the FDA decides to do on this score is emerging as a key issue for biopharma in 2017.

BY ED SCHOONVELD

Landmark 21st Century Cures legislation passed by Congress in December 2016 opens a potentially useful new chapter on the mission-critical question of how much evidence outside the standard randomized clinical trial the industry can share with the FDA in obtaining market authorization and subsequently with its commercial customers.

Explicit, well-corroborated proof of "value" involving multiple sources of information has become institutionalized in the commercial biopharma business, leaving the FDA as a blocking outlier to the trend.

To optimize the law's potential, companies want clarification from the FDA on what its expansive provisions mean in practice: will the agency come forward with the detailed specs to address numerous legal and procedural uncertainties – and how soon?

FDA's January 18 issue of a draft guidance on industry communication with payer is an initial step in this direction, but more work remains to be done.

The 21st Century Cures Act, enacted by Congress in December 2016, represents a watershed in the US regulatory approach to biopharmaceuticals. The law, which after two years of debate passed with strong bipartisan support, carries implications not only for the future funding of drug research, but also on the way the FDA uses medical data, advanced information technologies and patient experience for the approval of new medicines and the ability to disseminate health economic information.

Specifically, the act offers the opportunity to liberate what many FDA observers consider to be overly tight communication restrictions regarding clinical and economic evidence, as well as the incorporation of patient preferences in registration dossier evaluations. The big question for the industry is whether the FDA will step into the 21st century, where health care payer and provider organizations are making decisions involving economics and patient outcomes; where uncontrolled medical information is a primary purpose of Internet usage; and where the industry is prevented from communicating on economics and patient outcomes with key decision-makers of access and pricing. Will the law enable the implementation of meaningful risk-sharing deals, which often fail to materialize due to the uncertainty that provokes larger legal and compliance concerns?

Progress on these fronts would also address the curious contrast between the FDA's strict limits on communication between health care businesses under Section 114 of the Prescription Drug User Fee Act and uncontrolled medical communications through the Internet, where the FDA has long believed that a key public health constituency – the patient – may be at a risk.

Provisions Of The Act

The 21st Century Cures Act includes a large number of provisions related to health care:

- Funding for National Institutes of Health research programs for cancer research ($1.8 billion), brain research ($1.5 billion), precision medicine ($1.4 billion) and regenerative medicine ($30 million);

- The Precision Medicine Initiative to use genomic and other novel technologies to improve targeted prevention, diagnosis and treatment of disease; FDA acceptance of new drug development tools, such as biomarkers and clinical outcome assessments in drug reviews;

- Various FDA-related provisions that provide funding for regulatory process changes, antimicrobial innovation/stewardship, vaccine licensing and related staffing needs;

- Use of real-world evidence (RWE) and patient experience data (PED) in efficacy and safety evaluations, and drug marketing authorization approval decisions; and

- Authorization to disseminate health care economic information (HEI) to "a payer, formulary committee or other similar entity" responsible for "the selection of drugs for coverage or reimbursement."

The medical research funding provisions have attracted the most attention. They provide important room for advancement in cancer and mental health, along with better understanding of how precision medicine (previously referred to as "personalized medicine") can be used for a more targeted application of the available treatment options.

Hidden Impact: Expanding The FDA Evidence Base

The research-funding elements of the act, as important as they are to stimulating further advancement in the battle against existing and new debilitating diseases, may not be the most important driver of change in the long term. More clarity on broader use of RWE and PED in approvals – as well as the ability for drug companies to use HEI in communications with payers and formulary decision-makers – may have a stronger impact on how drug companies communicate value to customers through compelling evidence that enables differentiating value claims. These changes are a much-needed adjustment that could bring communications in line with the rapidly evolving needs of payer and provider organizations. Payers and providers are demanding stronger evidence of value in today's environment, but why would drug companies invest in these efforts if they are not considered by the FDA as relevant to the decision on marketing approval and if they are blocked by the FDA from communicating such value claims to their commercial customers? There are still some remaining questions, and opportunities for the FDA to provide clarification and thereby ensure that these intended changes in the 21st Century Cures Act are actually realized and don't falter over remaining concerns in the legal departments of the drug industry and their business customers.

Nevertheless, value communications to managed care organizations (MCOs), pharmacy benefit managers (PBMs), provider organizations and other key decision-makers and influencers are likely to face substantial changes under the act's provisions on real-world evidence, patient experience data and the dissemination of health care economic information.

As the FDA will be able to consider RWE and PED in drug evaluations, a more holistic assessment of the impact of a disease and treatment on patient lives could be done through observational studies, claims analyses and patient registries, thus overcoming some of the limitations of the randomized controlled clinical trial setting. In the past, the drug industry has been unable to communicate on these aspects of economic and patient outcomes value, although payers and evolving customers, such as integrated provider networks, are making many of their decisions on that basis. Let's take a closer look at how these changes in the US prescription drug market have impacted perceptions of value and evidence needs.

Today's Market Imperative: The Pursuit Of Value

Demonstration of value – particularly in economic and patient outcomes – has become critical to securing organizational and broader societal support for coverage of new drugs. It signifies a need for substantially more evidence of clinical, economic and patient outcomes value versus the standard of care. This constitutes a far step beyond the classical FDA-required randomized clinical trial comparisons with placebo. In many ways, the FDA lags behind the reality that drug manufacturers now face on the commercial side in proving value on how well a product performs not just at the bench, but at the bedside as well.

Exhibit 1 illustrates how the pharmaceutical industry needs to consider what I call the "dinner for three" decision dynamic between payer, physician and patient while at the same time address the value-evidence needs of "influencers" such as the medical profession, provider organizations, patient advocacy groups, employers, health technology assessment organizations, media, politicians and others. It shows how each of these stakeholders needs customized evidence that addresses their specific objectives and concerns. Some examples:

- Integrated delivery networks (IDNs) and accountable care organizations (ACOs) want to see impact on their quality metrics and their economics.

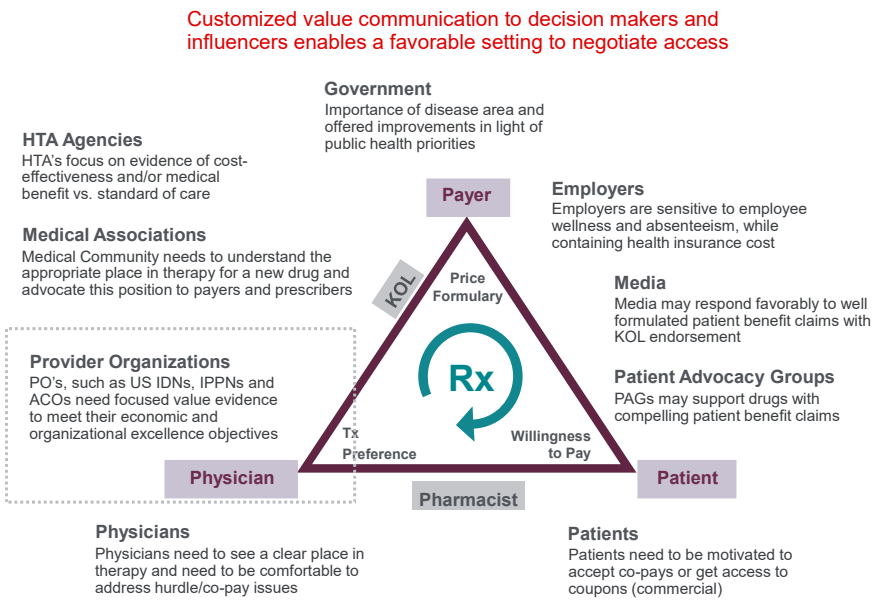
- Medical associates want to get evidence that helps decision-making in treatment guideline decisions, which increasingly determine which patient should get what treatment option.

- Prescribing physicians need to understand a drug's best place in overall therapy, as well as how to address any patient cost concerns.

As illustrated with these examples, the pharmaceutical industry needs to be aware of the particular objectives and evidence requirements of every individual stakeholder to ensure support in market access decisions and drug prescriptions. To do that, companies must drill down to include specific clinical, economic, patient-outcome and patient-satisfaction components. Through its expanded provision for these new forms of evidence, the 21st Century Cures Act will better enable a drug manufacturer to justify to the

Exhibit 1

Value Communication Needs Across Decision-Makers And Their Influencers



SOURCE: Schoonveld, The Price Of Global Health

payer and other stakeholders highlighted in Exhibit 1 why a new product should be granted access to the patient population through a formal reimbursement listing.

The How To: Analyzing Needs Of Decision-Makers And Influencers

A benefits analysis framework, described in detail in *The Price of Global Health (chapter 10)*, is a useful tool for analyzing the importance of potential claims to these stakeholders. Clinical, humanistic, economic and public health benefits are domains of benefits that particularly influence payer decision-making. Physicians and patients generally focus on clinical and humanistic benefits, usually supported with typical clinical trial endpoints (efficacy, tolerability) and quality-of-life metrics.

Exhibit 2 shows how some typical customers prioritize evidence of value across the benefits domains. The specific benefits (clinical endpoints, economic claims) within the domains can vary by customer, depending on, for example, their cost perspective and time horizon. Provider organizations, such as IDNs like Dean Health Plan or integrated physician provider networks (IPPNs) like Geisinger Health System, focus heavily on how their population health – as measured through various quality metrics – and economics are affected. ACOs are subject to a number of outcome metrics that are particularly focused on cardiovascular and diabetes endpoints, as well as general hospitalization and re-hospitalization metrics. These formal metrics, as well as patient satisfaction metrics, are captured under "organizational excellence" benefits. The oncology examples show the importance of public health benefits in this therapy area, as well as organizational excellence. Economics are critical as well, although to a lesser extent for the cancer hospitals, which have a broader scientific mission. The contrast between all of these institutions and the individual providers is clearly visible. Individual physicians are heavily focused on clinical and, to some extent, humanistic factors. As physicians are increasingly associated with larger IDNs, IPPNs and specialty provider clinics, such as the oncology super groups, this has big implications for evidence requirements that associate directly with the identification of positive health outcomes.

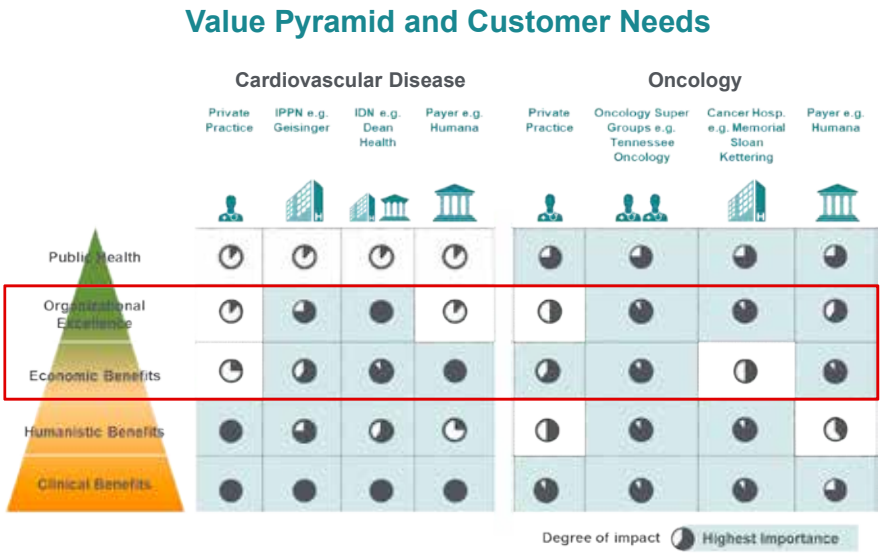
Let's look at some of the other stakeholders, such as payers and medical communities. A PBM may only be interested in pharmaceutical drug margin in terms of negotiated rebates. Since medical cost offsets due to better patient outcomes are not in their perspective, they will not consider them but rather simply focus on next year's total drug budget, their ability to pass that on to employers and the rebate revenues that they may be able to retain. MCOs will have a broader medical focus as they also cover non-drug medical cost, but given membership turnover, they're also likely to be focused on the short term (one to three years).

Medical communities are likely to be more focused on clinical and humanistic benefits but will ultimately focus on population-wide public health benefits, which may also attract more media attention. This illustrates the 180-degree difference between medical communities and PBMs.

The above examples illustrate how benefits and evidence needs can be very different between customers and across therapy areas. A closer analysis is therefore essential for each individual situation, which reinforces the usefulness of the act's new data provisions in assisting drug manufacturers to respond directly to each payer or provider's specialized evidence requirements.

The benefits analysis reveals that HEI, RWE and PED evidence are of high importance to many payers and perhaps more so for provider organizations. In the age of TripAdvisor and similar Internet tools, it's only a matter of time before health care providers are as heavily impacted as the restaurant industry. Hence it's critical to be able to show analyses to a payer or provider organization on how a new drug treatment will impact both the drug budget and medical expenditures overall. This analysis will be very different from customer to customer due to organizational type and focus differences, payment contract variations and differences in the population that the institution is serving. RWE is an important tool in gathering patient unmet needs information for populations within a disease area, but it can also provide long-term, post-launch data on how each drug treatment is performing. The caveat is that requiring this evidence at launch will prevent any new drugs from entering

Exhibit 2
Value Pyramid And Customer Needs



SOURCE: Schoonveld, The Price Of Global Health

the market. Therefore, regulators, payers and medical communities will need to continue to accept surrogate clinical endpoint data for new innovations.

Enabling health providers to make informed decisions on the impact of drug treatments on long-term patient outcomes requires the industry to undertake the appropriate studies, and to have the ability to show the data – and to talk about it.

Will The FDA Step Boldly Into The 21st Century?

The 21st Century Cures Act offers a real opening to broader communication on these topics. However, there's still an important task facing the FDA in clarifying what this means. What's really allowed now, and what's not? Which customers will qualify for more open communications on HEI? Payers and formulary decision-makers would logically include hospitals and also provider organizations, such as IDNs, IPPNs and ACOs. These customer groups are intensively focused on HEI and PED information, as well as RWE confirmation of improvement claims.

Industry compliance departments will be struggling with these questions well into 2017 and beyond. Until this is clarified, implementation of these new opportunities may be very slow.

A clarifying step in this direction has been taken in the form of a draft FDA guidance, "Drug and Device Manufacturer Communications with Payers, Formulary Committee and Similar Entities: Questions and Answers," issued on January 18. The document offers insight into several key aspects of the FDA evidence development process: the provision of information to payers for investigational drugs prior to approval, and what kind of non-label health economic information a drug manufacturer can share with formulary committees. It provides crucial, clarifying "safe harbor" protection from the existing prohibition on promotion of an investigational drug, allowing more flexibility for drug manufacturers to provide to payers certain information about such products in advance of FDA approval.

In Vivo's sister publication *The Pink Sheet* reports how the draft guidance provides more flexibility for manufacturers to communicate science-based information to payers. *(Also see "Industry Communications With Payors: US FDA Okays Info On Investigational Drugs" - Pink Sheet, 19 Jan, 2017.)* Addressing what evidence firms must have to support this health care information, the draft guidance states that FDA would not consider such information false or misleading if it relates to an approved indication and is based on "competent and reliable scientific evidence" (CARSE). The guidance adds that information would meet the CARSE designation if it was developed using generally accepted scientific standards that yield "accurate and reliable results."

Further, the text states that when evaluating information based on indirect treatment comparisons in the absence of data from head to head controlled clinical trials, FDA may refer to guidelines issued by external expert bodies covering methodologies and best practices for such comparisons. And finally, the draft notes that firms should also provide payers with information on the design, objectives and limitations of an economic analysis; the generalizability of the data; and a sensitivity analysis identifying any uncertainties that could affect the conclusions. Information on differences in the health care economic information from the FDA-approved labeling, omitted data sources and important risk information must be included, as well.

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